REMARKS

Claims 1-4, 6-14, 16, 19, 21, 23-26, 28-40, 56-68, 82 and 103-139 were pending in the application. Claims 1, 8, 82 and 113-116 have been amended. Claims 140-156 have been added. Claims 28 and 29 have been cancelled without prejudice. Therefore, claims 1-4, 6-14, 16, 19, 21, 23-26, 30-40, 56-68, 82 and 103-156 are currently pending in the application.

No new matter has been added. Support for the amendments to claims 1 and 82 can be found, for example, at least at page 7, lines 1-8 and page 22, line 1 through page 24, line 9 of the specification as originally filed. Claim 21 has been amended to clarify the invention. Support for new claims 140-156 can be found, for example, in the claims as originally pending and in the specification, as originally filed, at least at, for example, page 22, line 1 through page 24, line 9.

Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The cancellation of and/or amendments to the claims are not related to any issues of patentability.

Applicants gratefully acknowledge the Examiner's withdrawal of the rejections of the claims under the judicially created doctrine of obvious-type double patenting, and under 35 U.S.C. §112, second paragraph.

Applicants note with appreciation that claims 25, 26, 28, 29, 56-68, and 103-139 were found to be free of the prior art.

Co pending Applications

In addition to the applications listed in Applicants' information disclosure statement filed on June 8, 2006, Applicants would like to also bring the Examiner's attention to the related application, U.S. Application No. 11/657412, filed on January 24, 2007 which is also co pending with the current application.

Rejection of Claims 1-4, 6-14, 16, 19, 21, 23, 24, 30-40, and 82 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

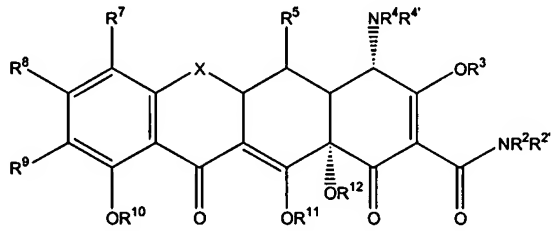
The rejection of claims 1-4, 6-14, 16, 19, 21, 23, 24, 30-40, and 82 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 26-54 of co pending Application No. 10/839,023.

While in no way admitting that the present claims are obvious over claims 1 and 26-54 of co pending application No. 10/839,023, upon allowance of the '023 application, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

Rejection of Claims 1-5, 11-13, 16, 18, 19 and 82 under 35 U.S.C. §103(a)

Claims 1-5, 11-13, 16, 18, 19 and 82 are rejected under 35 U.S.C. §103 (a) as being unpatentable over Barden *et al.*, "Glycylcyclines 3. 9-Aminodoxycyclinecarboxamides," *J. Med. Chem.*, 37(20):3205-11 (1994).

Claim 1 and its dependent claims are directed to substituted tetracycline compounds of the formula:



(I)

wherein:

X is $CHC(R^{13}Y'Y)$, $CR^{6'}R^6$, S, NR^6, or O;

R^2 is hydrogen, alkyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^4 and $R^{4'}$ are each hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$R^{2'}$, R^3, R^{10}, R^{11} and R^{12} are each hydrogen or a pro-drug moiety;

R^5 is hydrogen, hydroxyl, or a prodrug moiety;

R^6, $R^{6'}$, and R^8 are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, or halogen;

R^7 is hydrogen or $NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen;

R^{13} is hydrogen, hydroxy, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

Y' and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

R^9 is hydrogen, or $NR^{9c}C(=Z')ZR^{9a}$;

Z is O;

Z' is O or S;

R^{9a} is unsubsituted C_3-C_{10} alkyl, substituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkylthio, substituted or unsubstituted alkylsulfinyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted alkylamino, substituted or unsubstituted arylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic, substituted or unsubstituted heteroaromatic, absent, or a prodrug moiety, wherein said substituted alkyl is substituted with halogen, amino, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl; further wherein said substituted alkenyl, substituted alkynyl, substituted alkoxy, substituted alkylthio, substituted alkylsulfinyl, substituted alkylsulfonyl, substituted arylsulfonyl, substituted alkoxycarbonyl, substituted arylcarbonyl, substituted alkylamino, substituted arylalkyl, substituted aryl, substituted heterocyclic, or substituted heteroaromatic is substituted with halogen, amino, alkyl, alkenyl, alkynyl, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl;

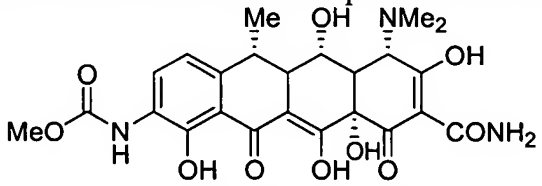
R^{9c} is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic or heteroaromatic;

W is $CR^{7d}R^{7e}$, NR^{7b} or O;

W' is O or S; and

R^{7a}, R^{7b}, R^{7c}, R^{7d}, and R^{7e} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic, absent, or a prodrug moiety, and R^{7d} and R^{7e} may be linked to form a ring; and pharmaceutically acceptable salts thereof, provided that at least one of R^9 is not hydrogen when R^7 is hydrogen or dialkylamino. Claim 82 is directed to pharmaceutical compositions comprising the compounds of formula (I).

In contrast, Barden *et al.* describes a compound of the formula:



The Examiner asserts that "[t]he instant claimed compounds would have been obvious [over Barden *et al.*] because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference." In addition, he states that since Barden *et al.* alleges that the potency of the compounds increased with additional alkyl groups on the amide chain, "one of ordinary skill in the art would be motivated to prepare compounds with larger groups bonded to the oxygen as well."

Applicants respectfully disagree. A skilled artisan would appreciate that even small modifications in chemical structure can effect the pharmacological activity, and therefore, even if the prior art teaches a methyl ester, a skilled artisan would not reasonably know that the ethyl ester would have similar pharmacological activity.

However, in the interest of expediting prosecution, Applicants' have amended the claims such that the compounds are substituted with substituents other than alkyl groups. Barden *et al.* neither teaches nor suggests the use of substituted alkyl groups, such as those currently claimed by Applicant.

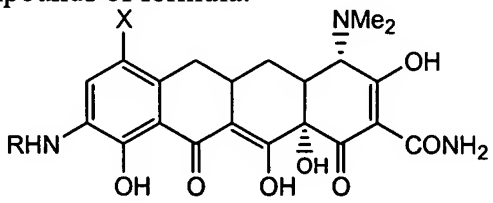
Applicants respectfully submit that the claims, as amended, are non-obvious over Barden *et al.* and request that this rejection of claims 1-5, 11-13, 16, 18, 19 and 82 under 35 U.S.C. §103 (a) be withdrawn.

Rejection of Claims 1-4, 6-8, 11-13, 16, 19, 21 and 82 under 35 U.S.C. §102(b)

Claims 1-4, 6-8, 11-13, 16, 19, 21 and 82 are rejected under 35 U.S.C. §102(b) as being anticipated by Hlavka *et al.*, U.S. Patent 5,494,903. Applicants respectfully traverse this rejection.

As described above, Applicants' claims 1 and 82 and their dependent claims are directed to tetracycline compounds of formula (I), wherein R^7 is hydrogen or $NR^{7c}C(=W')WR^{7a}$, and pharmaceutical compositions containing them.

Hlavka *et al.* describes compounds of formula:



wherein X is amino, NR^1R^2 or halogen.

Hlavka *et al.* only describes compounds wherein the X (e.g., the substituent which corresponds to Applicants' R^7) is amino, NR^1R^2 (wherein R^1 and R^2 are both independently hydrogen or alkyl) or halogen. Hlavka *et al.* does not teach or suggest tetracycline compounds wherein the substituent corresponding to R^7 is hydrogen or $NR^{7c}C(=W')WR^{7a}$, as claimed by Applicants.

Therefore, Applicants respectfully request that this rejection of claims 1-4, 6-8, 11-13, 16, 19, 21 and 82 under 35 U.S.C. §102(b), be withdrawn.

Rejection of Claims 1-4, 6-14, 16, 19, 21, 23-26, 28-40, 56-68, 82 and 103-139 under 35 U.S.C. §112, second paragraph

Claims 1-4, 6-14, 16, 19, 21, 23-26, 28-40, 56-68, 82 and 103-139 are rejected under 35 U.S.C. §112, second paragraph as being indefinite. In particular, the Examiner notes that "while the specification provides for examples of possible substituents [for R^{9a}], there is no way to determine the meets and bounds of the claims." The Examiner further states that "in order to overcome this rejection, the specific alternative substituents must be provided in the claims."

Applicants disagree. However, in the interest of expediting prosecution of the application, Applicants have amended the claims to recite the particular alternative substituents for R^{9a} in independent claims 1 and 82. The remainder of the rejected claims depend from claim 1 and thus contain all of its limitations.

Therefore, Applicants respectfully submit that this rejection of the claims under 35 U.S.C. § 112, second paragraph, no longer applies to the claims as amended, and respectfully request that it be withdrawn.

Rejection of Claims 1, 28 and 29 under 35 U.S.C. §112, first paragraph

Claims 1, 28 and 29 are rejected under 35 U.S.C. §112, first paragraph, as not being enabled for not reasonably providing enablement of compounds of formula (I), wherein R^{9a} is a steroid. Applicants respectfully submit that claims 28 and 29 have been cancelled, thus rendering their rejection moot and claim 1 has been as amended no longer include the compounds wherein R^{9a} is a steroid. Therefore, Applicants respectfully request that this rejection of claim 1 under 35 U.S.C. § 112, first paragraph be withdrawn.

SUMMARY

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conference with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: June 21, 2007

Respectfully submitted,

By _____

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